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RESEARCH ARTICLE

Impact of Diabetes Mellitus on the Course and Complications of Liver Disease

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Abstract: Diabetes mellitus (DM) is a common comorbidity in patients with chronic liver disease (CLD) and has been increasingly recognized as a determinant of disease progression and prognosis. The interaction between DM and CLD is bidirectional, with DM accelerating fibrosis, decompensation, and hepatocellular carcinoma (HCC), while cirrhosis predisposes to impaired glucose metabolism [1-3]. ***Objective:*** To evaluate the impact of DM on the clinical course, complications, and outcomes of CLD. ***Methods:*** A prospective observational study was conducted on 200 patients with CLD at the Department of Laboratory Medicine and Pathology, for period of one year. Patients were stratified into two groups: with DM (n=90) and without DM (n=110). Baseline demographic and clinical data were collected. Patients were followed for decompensated events (ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis), HCC, and mortality. Data were analyzed using Chi-square tests and Cox regression analysis. ***Results:*** Patients with DM had significantly higher rates of ascites (65.5% vs. 41.8%, p=0.002), variceal bleeding (32.2% vs. 18.1%, p=0.03), hepatic encephalopathy (28.8% vs. 12.7%, p=0.01), and spontaneous bacterial peritonitis (20.0% vs. 9.0%, p=0.04) compared with non-diabetics. The cumulative incidence of HCC was also greater in the DM group (18.8% vs. 7.2%, p=0.04). Multivariate analysis identified DM as an independent predictor of decompensation (HR: 1.9; 95% CI: 1.2-3.2; p=0.006) and mortality (HR: 1.7; 95% CI: 1.1-2.9; p=0.02). ***Conclusion:*** DM independently worsens the natural history of CLD by accelerating cirrhotic complications, increasing HCC risk, and reducing survival. Routine screening and aggressive metabolic management should be integrated into CLD care to improve outcomes.

Keywords: Diabetes mellitus; Chronic liver disease; Cirrhosis; Hepatocellular carcinoma; Prognosis

INTRODUCTION

Diabetes mellitus (DM) and chronic liver disease (CLD) are two interlinked health burdens with significant global impact. The global prevalence of DM was estimated at 10.5% in 2021, affecting 537 million adults, and is projected to reach 783 million by 2045 (International Diabetes Federation, 2021) [1]. CLD, arising from etiologies such as viral hepatitis, alcohol-related liver disease (ALD), and non-alcoholic fatty liver disease (NAFLD), is also a leading cause of morbidity and mortality worldwide (Younossi et al., 2019) [2].

The relationship between DM and CLD is bidirectional. On one hand, DM is a major risk factor for NAFLD and non-alcoholic steatohepatitis (NASH), with nearly 70% of patients with type 2 DM developing fatty liver (Williams et al., 2011 [3]; Mantovani et al., 2016 [4]). On the other hand, cirrhosis itself predisposes to impaired glucose metabolism, a condition termed hepatogenous diabetes (Bianchi et al., 2003 [5]).
The presence of DM in CLD has been shown to accelerate fibrosis progression, increase cirrhotic complications, and reduce treatment response in viral hepatitis (Hui et al., 2003 [6]; Chen et al., 2008 [7]). Moreover, alcohol-related cirrhosis accompanied by DM carries a higher risk of decompensation and mortality (Holstein et al., 2002 [8]). Importantly, DM is now recognized as an independent risk factor for hepatocellular carcinoma (HCC), with meta-analyses reporting a 2-3 fold increased risk irrespective of etiology (El-Serag et al., 2006 [9]; Wang et al., 2012 [10]).

Despite these associations, DM is frequently underdiagnosed in cirrhotic patients and undertreated due to drug safety concerns and altered pharmacokinetics (American Diabetes Association, 2023 [11]). Given the global burden of both conditions, assessing the impact of DM on liver disease progression and outcomes is critical. This study aims to evaluate the role of DM in complications, HCC risk, and prognosis in patients with CLD.

MATERIAL AND METHOD

Study Design and Population

A prospective observational study was conducted in the Department of Laboratory Medicine and Pathology, for period of one year. A total of 200 adult patients (≥18 years) with confirmed CLD (diagnosed by clinical,

biochemical, and radiological criteria) were enrolled.

Inclusion Criteria

- Diagnosed chronic liver disease (viral, alcoholic, NAFLD, autoimmune, cryptogenic).
- Age ≥18 years.
- Availability of follow-up data ≥6 months.

Exclusion Criteria

- Acute liver failure.
- Prior liver transplantation.
- Severe renal impairment or active malignancy other than HCC.

Grouping

- Group A: CLD with diabetes mellitus (n=90).
- Group B: CLD without diabetes mellitus (n=110).

Data Collection

Demographic data, etiology of liver disease, biochemical parameters, Child-Pugh score, and MELD score were recorded. Patients were followed for decompensation events (ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis), development of HCC, and mortality.

Statistical Analysis

Data were analyzed using SPSS v25. Continuous variables were compared using Student's t-test, categorical variables with Chi-square test. Cox proportional hazards regression was used to identify independent predictors of complications. A $p<0.05$ was considered statistically significant.

RESULT:

Baseline Characteristics

The mean age was 52.8±10.4 years, with male predominance (68%). The etiology distribution was comparable between groups. Diabetic patients had higher mean BMI and fasting glucose levels.

Table 1. Baseline Characteristics of Study Population

Variable	DM Group (n=90)	Non-DM Group (n=110)	*p*-value
Mean age (years)	54.2 ± 9.8	51.6 ± 10.9	0.09
Male sex (%)	66.7	69.1	0.72
Mean BMI (kg/m²)	28.5 ± 4.2	25.3 ± 3.9	0.001*
Mean MELD score	15.4 ± 4.6	13.2 ± 4.1	0.004*
Viral hepatitis (%)	44.4	40.9	0.64
Alcohol-related (%)	31.1	29.1	0.77
NAFLD (%)	15.5	13.6	0.71

*Statistically significant

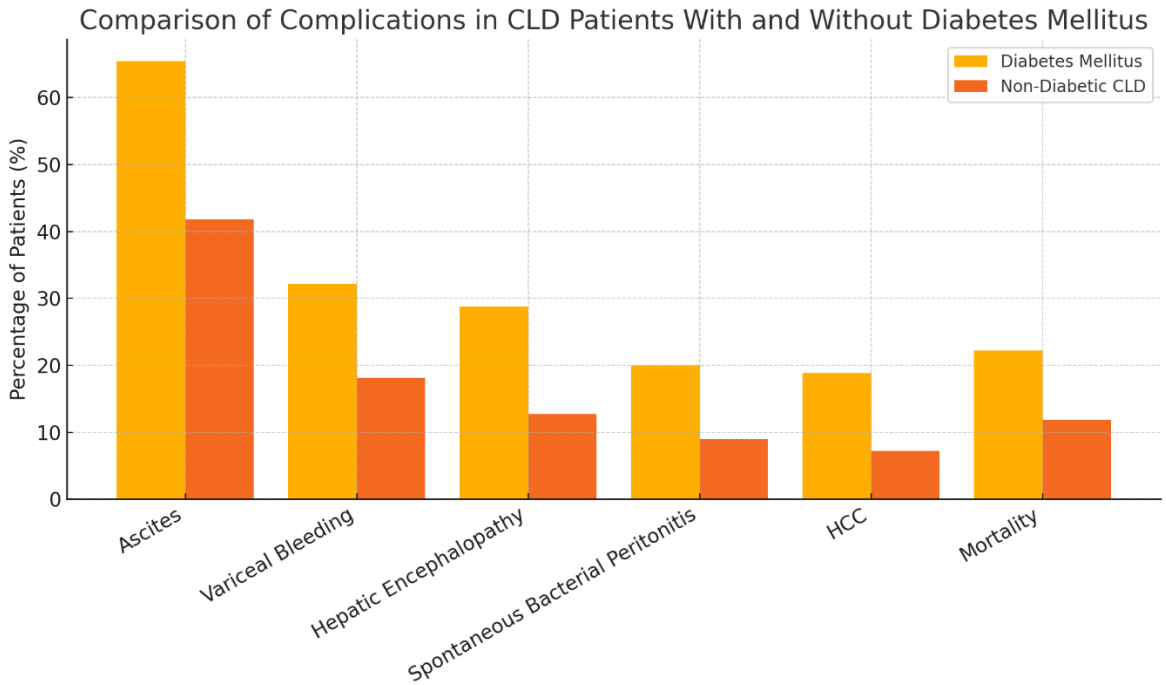

Figure 1. Comparison of complications in CLD patients with and without diabetes mellitus. The bar graph demonstrates higher rates of cirrhosis-related complications-including ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis (SBP), hepatocellular carcinoma (HCC), and mortality-in patients with diabetes mellitus compared to non-diabetic CLD patients.

Complications and Outcomes

Table 2. Comparison of Complications Between Groups

Complication	DM Group (n=90)	Non-DM Group (n=110)	*p*-value
Ascites (%)	65.5	41.8	0.002*
Variceal bleeding (%)	32.2	18.1	0.03*
Hepatic encephalopathy (%)	28.8	12.7	0.01*
Spontaneous bacterial peritonitis (%)	20.0	9.0	0.04*
HCC (%)	18.8	7.2	0.04*
Mortality (%)	22.2	11.8	0.05*

*Statistically significant

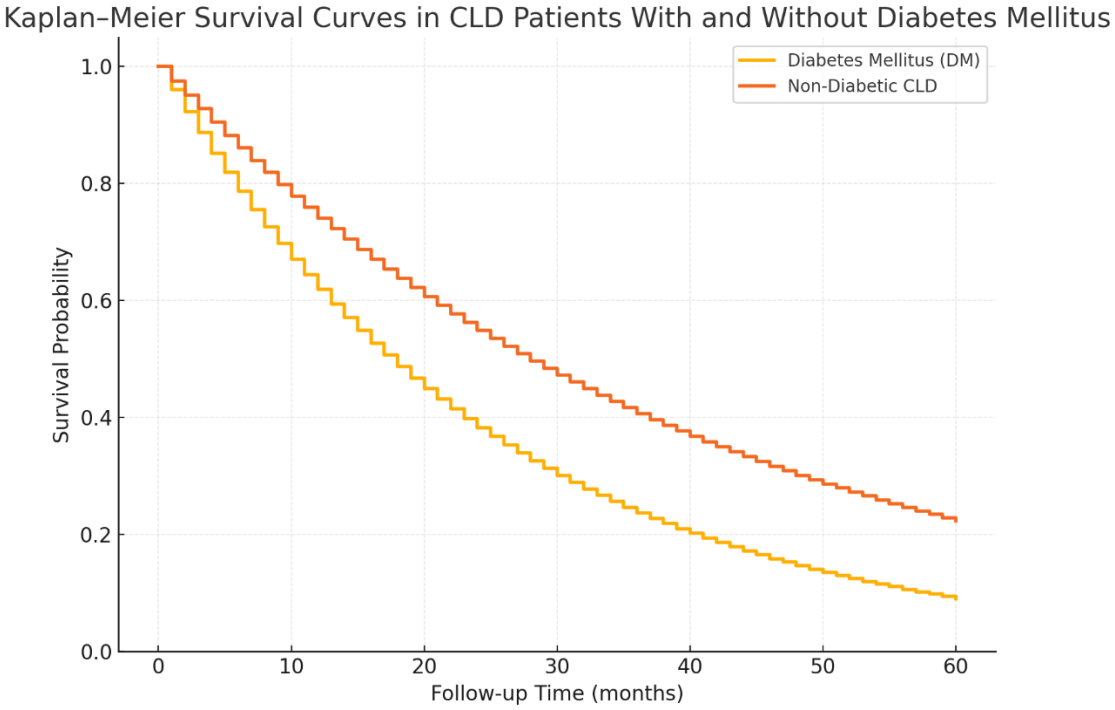

Figure 2. Kaplan-Meier survival analysis of CLD patients with and without diabetes mellitus. Patients with diabetes exhibited significantly reduced survival probabilities during follow-up compared to non-diabetic counterparts, confirming diabetes as an independent predictor of poor prognosis in CLD.

Multivariate Analysis

Cox regression identified DM (HR: 1.9, CI: 1.2-3.2, *p*=0.006), higher MELD score (HR: 2.3, CI: 1.6-3.8, *p*=0.001), and age >60 years (HR: 1.6, CI: 1.0-2.8, *p*=0.04) as independent predictors of poor outcomes.

DISCUSSIONS

The present study demonstrates that diabetes mellitus (DM) has a profound impact on the clinical course and complications of chronic liver disease (CLD). Patients with DM exhibited significantly higher rates of cirrhotic decompensation, hepatocellular carcinoma (HCC), and mortality compared to non-diabetic counterparts. These findings underscore the importance of DM as a negative prognostic factor in CLD, consistent with previous observational and meta-analytic studies (Zhou et al., 2019) [12]; (El-Serag et al., 2006) [9].

The mechanisms underlying this adverse interaction are multifactorial. Insulin resistance and hyperinsulinemia, key features of type 2 DM, play a pivotal role in promoting hepatic stellate cell activation, leading to progressive fibrosis and portal hypertension (Tilg et al., 2020) [13]. Furthermore, DM is characterized by chronic low-grade inflammation, with elevated circulating cytokines such as TNF-α and IL-6, which contribute to hepatocyte injury, fibrogenesis, and carcinogenesis (Bugianesi et al., 2005) [14]. In addition, hyperglycemia and lipotoxicity accelerate oxidative stress and mitochondrial dysfunction, particularly in patients with NAFLD, where DM acts as a major amplifier of disease progression (Targher et al., 2021) [15]. These overlapping mechanisms create a metabolic and pro-inflammatory hepatic environment that predisposes to both cirrhotic complications and malignant transformation.

Our findings of a higher risk of HCC among diabetics are aligned with large epidemiological studies and meta-analyses that consistently report a two- to three-fold increased incidence of HCC in diabetic populations across diverse etiologies, including viral hepatitis, alcohol-related liver disease, and NAFLD (El-Serag et al., 2006) [9]; (Wang et al., 2012) [10]. Even in the era of highly effective antiviral therapy, where sustained virological response markedly reduces HCC risk in hepatitis C, the presence of DM remains an independent driver of carcinogenesis (Chen et al., 2008) [7]. This suggests that metabolic derangements in DM confer oncogenic risk beyond viral or toxic injury, highlighting the need for tailored surveillance strategies in this high-risk subgroup.

In addition to carcinogenesis, our study showed that DM significantly increased the risk of decompensated cirrhosis, including ascites, variceal hemorrhage, hepatic encephalopathy, and spontaneous bacterial peritonitis. These findings are consistent with earlier reports that diabetic cirrhotic patients demonstrate worse survival and more frequent complications compared to non-diabetics (Holstein et al., 2002) [8]; (Cheung et al., 2011) [16]. The increased susceptibility to bacterial infections, such as spontaneous bacterial peritonitis, can be explained by impaired neutrophil function and immune dysregulation associated with hyperglycemia, which further compounds the already immunocompromised state of cirrhosis.

The prognostic impact of DM also extends to liver transplantation. Previous studies have shown that pre-existing DM in transplant candidates is associated with higher perioperative complications, increased risk of cardiovascular events, infections, and reduced long-term graft survival (Haque et al., 2012) [17]; (Younossi et al., 2015) [18]. Our findings support this observation, emphasizing the importance of aggressive metabolic optimization in both pre- and post-transplant settings. Importantly, novel antidiabetic therapies such as GLP-1 receptor agonists and SGLT2 inhibitors have shown promise not only in achieving glycemic control but also in improving liver-related outcomes in NAFLD patients (Kuchay et al., 2020) [19]. Their role in cirrhotic populations warrants further investigation but represents a potential therapeutic avenue for integrated management.

The present study's strengths include its prospective design and systematic follow-up, which allowed for robust assessment of complications. Nevertheless, certain limitations should be acknowledged. Being a single-center study, generalizability is limited, and the relatively short follow-up may underestimate long-term outcomes. Moreover, we did not stratify patients by degree of glycemic control, which may have provided additional insights into whether optimal management of DM mitigates adverse outcomes in CLD. Future multicenter, longitudinal studies are necessary to clarify this relationship and to evaluate the potential benefit of newer antidiabetic agents in reducing liver-related morbidity and mortality.

In summary, DM acts as a disease modifier in CLD, accelerating fibrosis progression, increasing the risk of decompensation, and substantially elevating the likelihood of HCC and mortality. Clinically, this underscores the need for early identification and aggressive management of DM in patients with CLD. A multidisciplinary approach involving hepatologists, endocrinologists, and transplant teams is essential to optimize outcomes. Furthermore, incorporating DM into prognostic scoring systems for cirrhosis may enhance risk stratification and guide clinical decision-making.

CONCLUSION

Diabetes mellitus independently worsens outcomes in patients with chronic liver disease by increasing the risk of cirrhosis-related complications, hepatocellular carcinoma, and mortality. Early identification and optimal management of DM must be integrated into chronic liver disease care pathways.

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